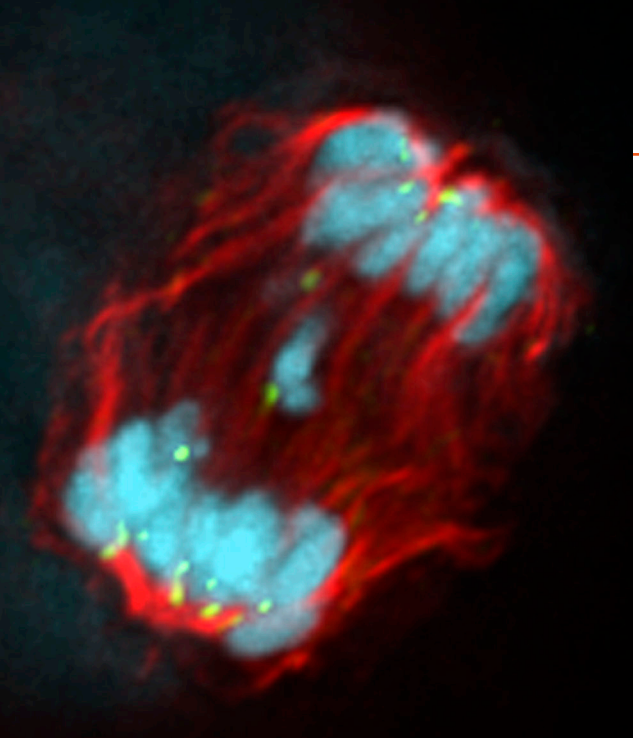

A chromosome (blue) whose kinetochore (green) is attached to spindle microtubules (red) from both poles lags behind during mitosis and creates aneuploidy.

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Losing odd chromosomes

Cancer cells need a little something extra to propagate with unusual chromosome numbers, based on evidence from Thompson and Compton.

Many tumors are packed with cells that have too many or too few chromosomes—a state known as aneuploidy. In theory, aneuploidy is the result of chromosome segregation errors during mitosis. The authors now identify one mechanism behind these errors: anaphase starts up while chromosomes are wrongly attached to both poles.

For proper segregation, sister chromatids of each chromosome should attach to opposite poles. But in several cancer cell lines, chromatids were often hitched to both poles during division, resulting in daughter cells with either both copies of a chromosome or neither.

Chromosome attachment is monitored by the spindle checkpoint, but this mechanism only stalls anaphase when it recognizes unattached chromosomes; it does not sense chromatid attachment to both poles. How they are prevented in normal cells is not yet known but probably involves microtubule detachment by aurora kinase.

Even with high segregation error rates, diploid cancer cell lines failed to maintain abnormal chromosome numbers. In two diploid lines, newly formed aneuploid cells were rapidly lost over subsequent generations. Perhaps aneuploid cells undergo apoptosis or senescence or are simply too slow-growing to compete with their diploid neighbors.

The authors now want to determine how aneuploid tumor cells keep their mismatched chromosome sets. Once their secret is identified, it might prove to be a therapeutic target that is unique to the tumor. JCB

Thompson, S.L., and D.A. Compton. 2008. *J. Cell Biol.* 180:665–672.

An adhesion kinase on centrosomes

New results from Fielding et al. place a kinase found in focal adhesions on centrosomes. There, the kinase helps arrange microtubules rather than actin.

Focal adhesions contain a mass of proteins that link matrix-bound integrins to the actin cytoskeleton. Within that mass is integrin-linked kinase (ILK), which phosphorylates other focal adhesion proteins during cell spreading and migration. While searching for ILK binding partners, Fielding and colleagues fished out an unexpected class of cytoskeletal proteins—tubulins.

In addition to α- and β-tubulin, several centrosomal microtubule-binding proteins were identified. The localization of active ILK and its partners to centrosomes was necessary for proper spindle formation during mitosis. The absence of ILK disrupted a complex of centrosomal proteins that includes Aurora A. In these cells, microtubules polymerized from only one pole and did not reach the DNA.

Although it is not clear how ILK creates a bipolar spindle, the authors hypothesize that it might be needed for centrosome duplication before mitosis. They are now using a proteomics approach to identify centrosomal targets of the kinase. JCB

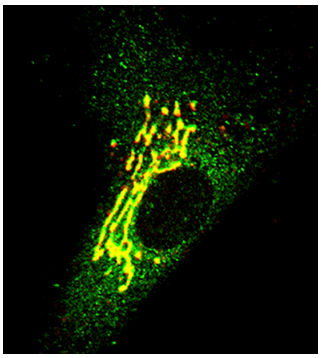
Fielding, A.B., et al. 2008. *J. Cell Biol.* 180:681–689.

Matching traffic and growth

The shuttling of a phosphatase keeps membrane trafficking in tune with cell growth, say Blagoveshchenskaya et al. The enzyme's removal from the Golgi increases trafficking when cells need it most.

Growing cells need new proteins and lipids delivered to the expanding plasma membrane. The outward transport of these components from the Golgi is driven in part by a pool of PI4P phospholipid, which is thought to help create a suitable lipid environment for the formation of Golgi-derived carriers. The new findings reveal that Golgi PI4P levels rise when cells get a taste of extracellular growth factors.

In dormant cells, PI4P levels at the Golgi were kept low by a phosphatase called SAC1, which turns PI4P to PI. To reach the Golgi, SAC1 formed oligomers that seem to uncover a binding motif that recruits it into ER-to-Golgi transport vesicles.



SAC1 (green) limits membrane trafficking from the Golgi (red) until cells are stimulated into proliferation.

The oligomers were disrupted when cells were given growth factors to jolt them out of dormancy. Both FGF and PDGF activated the ERK1/2 and p38 MAPK pathways, which led to disassembly of SAC1 oligomers. Collapse of the oligomers caused SAC1 relocation to the ER, thereby allowing Golgi PI4P levels to rise.

Constitutive activation of p38 was enough to nudge cells out of quiescence and back into proliferation, as occurs during early stages of cancer. The group will soon test whether SAC1 is necessary for this rejuvenation. JCB

Blagoveshchenskaya, A., et al. 2008. *J. Cell Biol.* 180:803–812.